DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Res
1401 Rockville Pike
Rockville MD 20852-1448

54494d

December 23, 2003

CBER-04-003

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mark W. Shinabery, P.D.
Director of Pharmacy Operations
Custom Compounding Centers
904 Autumn Road, Suite 275
Little Rock, Arkansas 72211

Dear Dr. Shinabery:

The Food and Drug Administration (FDA) has completed its review of the inspection conducted on August 29, 2003, of your facility, Custom Compounding Centers (CCC), located at 904 Autumn Road, Suite 272, Little Rock, Arkansas. The inspection revealed serious violations of the Federal Food, Drug, and Cosmetic Act (Act) and the Public Health Service Act (PHS Act).

As you may be aware, Section 127 of the FDA Modernization Act of 1997 amended the Act creating Section 503A, "Application of Federal Law to the Practice of Pharmacy Compounding." This provision became effective on November 21, 1998, and set forth the requirements that compounded products must meet to qualify for exemption from the new drug (505), certain adulteration (501(a)(2)(B)), and misbranding (502(f)(1)) provisions of the Act.

On February 6, 2001, the United States Court of Appeals for the Ninth Circuit held that the commercial speech restrictions in Section 503A violate the First Amendment to the Constitution, and further held Section 503A to be invalid in its entirety because the speech restrictions could not be severed from the remainder of the provision. On April 29, 2002, the Supreme Court affirmed the Ninth Circuit Court of Appeals decision. The Court did not rule on, and therefore left in place, the Ninth Circuit's holding that the unconstitutional restrictions on commercial speech could not be severed from the rest of Section 503A. Accordingly, all of Section 503A is now invalid.

Because of the Supreme Court decision, FDA determined that it needed to issue guidance to the field and compounding industry on what factors the agency will consider in exercising its enforcement discretion regarding pharmacy compounding. This guidance issued on June 7, 2002, in the form of Compliance Policy Guide, Section 460.200.

As a result, FDA now utilizes its longstanding policy to recognize and exercise its enforcement discretion for extemporaneous compounding, where reasonable quantities of drugs are manipulated upon receipt of valid prescriptions from licensed practitioners for individually identified patients. FDA remains seriously concerned, however, about the public health risks associated with the large-scale production of drug products without these products being required to meet all the laws and regulations applicable to a drug manufacturer.

Your firm purports to be a compounding pharmacy for an activator kit containing [redacted] for reconstitution. Documents collected during the inspection of CCC indicate that CCC receives the [redacted] from SafeBlood Technologies, Inc. However, our investigation has determined that your firm exceeds the scope of the regular course of the practice of pharmacy and into the activities of a drug manufacturer. For example, you manufacture the above drug product in anticipation of receiving prescriptions. You ship the kits to customers and fail to reconcile or account for the amount shipped with any prescriptions received from customers.

In light of the above, we do not believe that your firm is operating as a retail pharmacy engaged in extemporaneous compounding that would justify our exercising enforcement discretion. As such, your firm appears to be in violation of the following sections of the Act and the PHS Act:

351 of the PHS Act

The activator kits manufactured by your firm are biologics within the meaning of Section 351 of the PHS Act. As such, in order to introduce these kits or deliver them for introduction into interstate commerce, a valid biologics license (BLA) must be in effect for this product. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, biologic products may be distributed for clinical use in humans only if the sponsor has on file an investigational new drug application (IND) in effect as specified by the regulations (21 CFR Part 312). Based on a review of our files, FDA has no information that the product, "activator kit," is the subject of an approved BLA or subject to an IND. Therefore, your shipments of product for which a valid license or IND is not in effect represent violations of the PHS Act and the Act and may result in FDA seeking such relief as provided by law.

The activator kits manufactured by your firm are biologics within the meaning of Section 351(i) of the PHS Act because they are applicable to the treatment or cure of disease. The kits are labeled as "manufactured for SafeBlood," and information obtained during the inspection indicates that your firm manufactures these kits for SafeBlood Technologies of

Little Rock, Arkansas (SafeBlood). SafeBlood promotes the use of the activator at www.SafeBloodTech.com for the stabilization and application of an autologous tissue graft for the treatment of both acute and chronic wounds.

Section 502 (f)(1) of the Act and Section 351(a) of the PHS Act

Your drug product is misbranded within the meaning of Section 502(f)(1) of the Act in that its labeling fails to bear adequate directions for use for which it is being offered and it is not exempt from this requirement under 21 CFR 201.115. Additionally, your unlicensed biologic violates the labeling provisions of the PHS Act in that its labeling fails to bear the name, address, and license number of the manufacturer of the biologic.

Section 501(a)(2)(B) of the Act

Your drug product is adulterated within the meaning of Section 501(a)(2)(B) of the Act in that the controls and procedures used in the manufacture, processing, packing, and holding do not conform to current good manufacturing practices regulations, 21 CFR, Part 210 and 211. Deviations from these regulations include, but are not limited to, the following:

1. Failure to conduct for each batch of drug product appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release [21 CFR 211.165(a)] in that CCC has not performed any release testing;

2. Failure to maintain and/or follow a written testing program designed to assess the stability characteristics of drug products [21 CFR 211.166(a)] in that CCC has not performed any stability testing nor does a stability program exist;

3. Failure to assure that the drug product meets applicable standards of identity, strength, quality, and purity at the time of use [21 CFR 211.137(a)] in that the [redacted] expiration date established for the activator kit was not determined by appropriate stability testing;

4. Failure to maintain and/or follow written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess and to assure that such procedures, including any changes, are drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit [21 CFR 211.100] in that CCC has no standard operating procedures in place for manufacture of the activator kits. A worksheet with hand written instructions is used for the preparation of the activator kits;

5. Failure to maintain and/or follow written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures [21 CFR 211.80] in that CCC has no procedures in place for the receipt, identification, storage, handling,

sampling, testing, and approval or rejection of [redacted], and the product containers and closures;

6. Failure to retain and store under conditions consistent with product labeling an appropriately identified reserve sample that is representative of each lot or batch of drug product [21 CFR 211.170(b)] in that no retention samples are maintained.

This letter is not intended to be an all-inclusive list of the deficiencies that may exist at your facility. It is your responsibility to ensure that your operations are in compliance with all requirements of the federal regulations. You should take prompt action to correct the violations noted above. Failure to promptly correct these violations may result in regulatory action such as seizure and/or injunction without further notice.

Please notify this office in writing within 15 working days of receipt of this letter of any steps you have taken or will take to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your response should be sent to the U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448, Attention Mr. Steven Masiello, Director, Office of Compliance and Biologics Quality.

Sincerely,

for

Steven A. Masiello
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research